

1/15

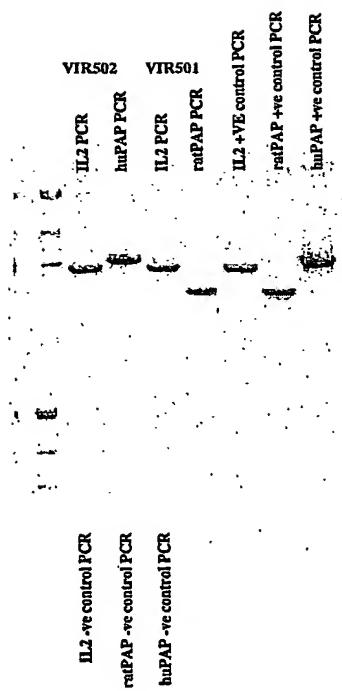
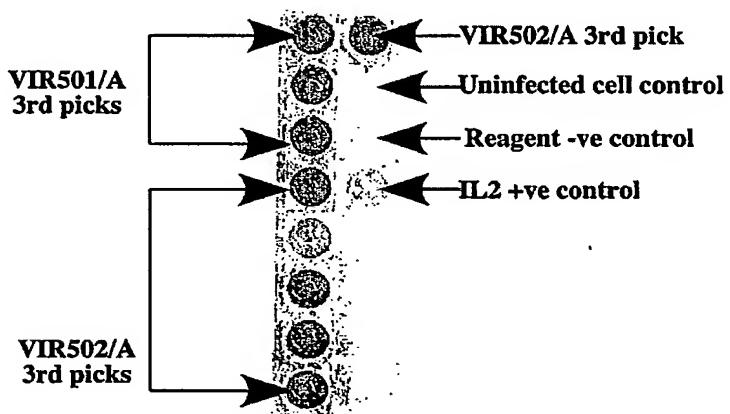


FIGURE 1

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**VIR501 and VIR502 third round plaque picks  
IL2-ELISA testing of undiluted culture medium from T25 infections**



**FIGURE 2**

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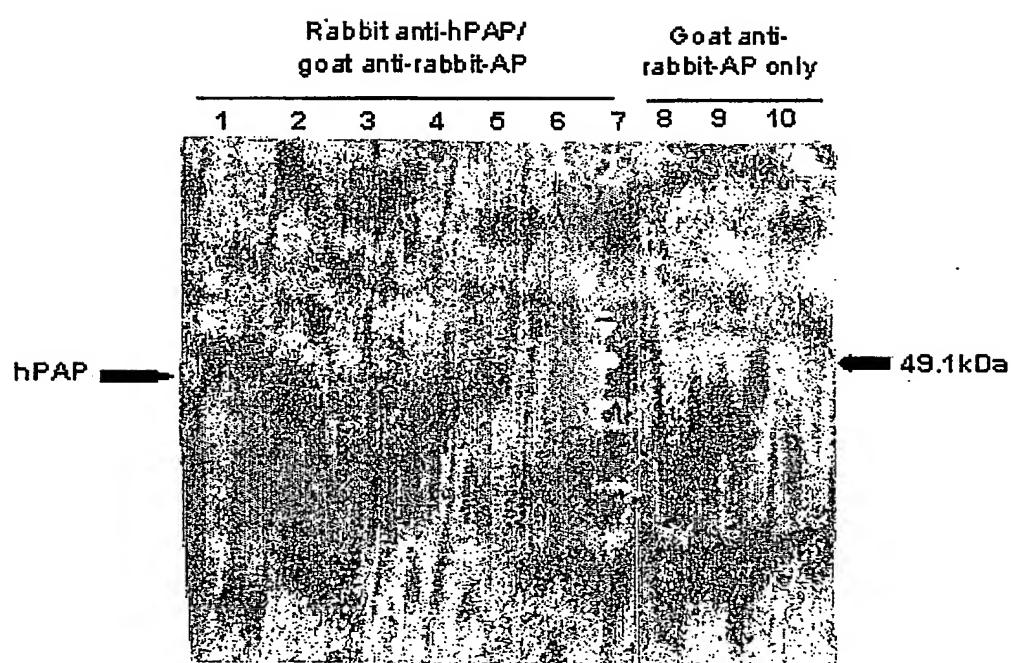
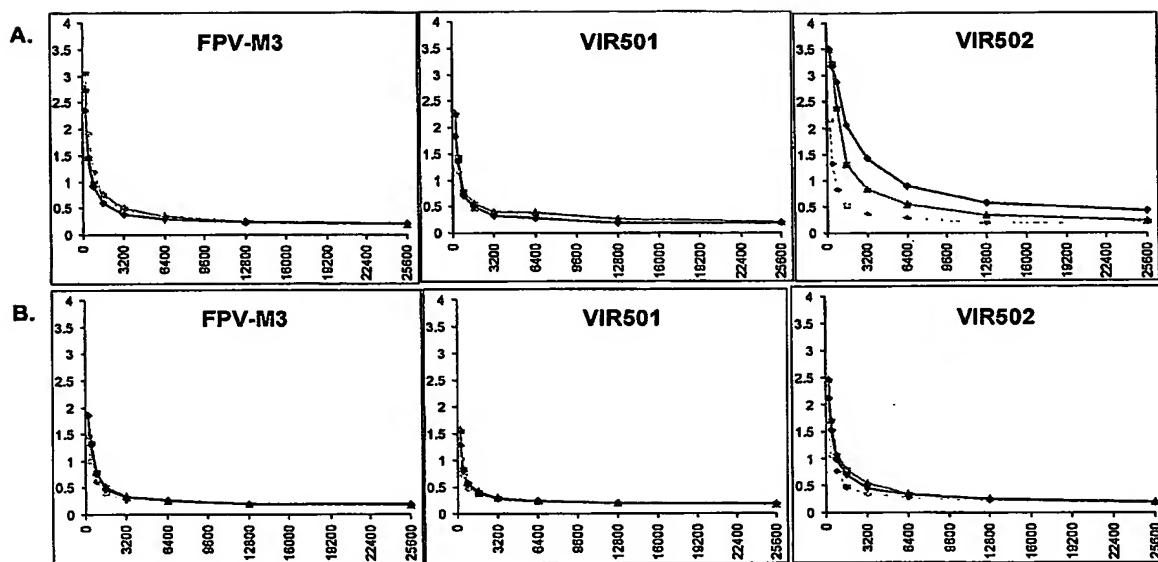


FIGURE 3

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**FIGURE 4**

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### Insertion site of VIR501 containing human IL2 and rat PAP sequences

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

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ATGGATAGAAATATCAATTAGTCTGTATTATAGAACCTAGGTTAACACAGAGTTCTATTATCCTCAAAGGTATTT
TACCTATCTTATAGTAAAATCAGGACATAAATCTGGATCCAATTGTGCTAAAGATAATAGAGGAGTTCCATAAAAA
TATATATTAGTTTGAAAGTAATAGTAGCTTGATTATATTGAATTTCCTTAAGGAAGAAATTATATACATTTTCCG
ATATATAATCAAAAACCTCATTATCATCGAAACTAATATAACTAAAAAGAAATTCTCTTATAATATGTAAAAAGGC
FPV132R ORF in bold →

TTAGCTAACGCTCTAAAAATTCAATAAATAGTCTGCTGGATAGAACTATGTTAAAGTGAAAGAAGATGGATCTTGATGATT
AATCGATTGGAAGATTTTAAGTTATTCAGACGACCTATCTGATACAATTACACTCTCTACCTAGAAACTACTAA

TCGAGACCTCCGGATCTATTGGCCTTGAGTTAGATGGTCACCGTAAGGATTTCCGATTGTAGTTGCTTTATCGTCA
AGCTCTGGAAGGCCATAGATAAGCCGGAACTCAAATCTACCAAGTGGCATTCTAAAGGCTAACATCAAACGAAAATAGCAGT

ATAATGGCGCATCCTCATCAACATCTCCTACTCTATTAAACAGACGATAACGGATTTATTCTTATCTATCCGAAAAAAG
TATTTACCGCGTAGGAGTAGTTGAGGAAATGAGATAAAAATTGTCTGCTATTGCTAAATAAGAATAGATAGGCTTTTC

TGATGATGAAGCTCTGAAGACATAAAACTATTAAGAAATATATGGACTTTATTCTAACGTTCTTACGTTCTAAAGAGAA
ACTACTACTCGAGAACTCTGTATTATGATAATTCTTATATACGAAATAAGATTGCAAGAATATGCAAGATTCTCTT

ACTAGAAAATATAGGATGTTCTTACCGCCTATGAGTGAATCGTTAAGGCTCTTAAAGTAAAGGATGATGGTACTTTAGT
TGATCTTTATATCCTACAAGAATGCTCGGAACTCACTTAGCAAATTCCGAGAATAATTCTACTACCATGAAATCA

AAAAGCATTACCAAGCCATTGTTAAATCCTCATTCCGAAAAGATAGTTTAGATAGAGGTTAACTTCGGATTTGCTATAAG
TTTCGTAATGGTCGGTAACAATTAGGAGTAAGGCTTCTATCAAATCTTCAATATGAAGGCCATTGTTATGTTATGTTAGGTTGCTCTTACATGAAATTC

CGTAATAAGACTATCTAGAAAAGCAGTTATATACCTCCGCAAATACAAAATACATAATCCAAACGAGAATATGTATATAAA
GCATTATTCTGATAGATCATTTCGTCATATATGAAGGGCGTTATGTTATGTTAGGTTGCTCTTACATATATAATT

CAACCTAATATCACTACTGAAGCGCAACTAGATCTCCAAACCCACCCGCTTTTATAGTAAGTTTCAACCCATAATAATAAA
GTTGGATTATAGTGTGACTTCGCGTTGATCTAGAAGGTTGGGTGGCGAAAATATCATTCAAAAAGTGGTATTATTATT
vaccinia p7.5 promoter in bold & italic →

ATACAATAATAATTCTCGTAAAGTAGAAAATATATTCTAATTATGTCACGGCTAGAACTAGTGatccATGTACAGGAT
TATGTTATTAAATTAAAGAGCATTTCATCTTTATATAAGATTAAACGTGCCAGATCTGATCACtaggTACATGTCCTA
> M Y R M

GCAACTCCTGCTTGCATTGCACTAATTCTGCACTTGTACAAACAGTCACCTACTTCAAGTCACAAAGAAAACAAAGAA
CGTTGAGGACAGAACGTAACGTGATTAAGAACGTGAAACAGTGTACGGTGTGACGTGGATGAAGTCAAGCTGTTCTTTGTTCTT
> Q L L S C I A L I L A L V T N S A P T S S S T K K T K K
human IL2 protein coding sequence →

AACACAGCTACAACGGGAGCATTTACTGCTGGATTACAGATGATTTGAATGGAATTAAATTACAAGAATCCCAAACCTCAC
TTGTGTCGATGTTGACCTCGTAAATGACGACCTAAATGTCTACTAAACCTACCTTAATTATTAATGTTCTAGGTTGAGTG
> T Q L Q L E H L L D L Q M I L N G I N N Y K N P K L T

CAGGATGCTCACATTAAAGTTTACATGCCAAGAAGGCCACAGAACTGAAACAGCTTCAGTGTCTAGAAGAAGAACTCAAAC
GTCCTACGAGTGTAAATTCAAAATGTACGGGTCTTCCGGTGTCTGACTTGTGCAAGTCACAGATCTCTTCTGAGTTGG
> R M L T F K F Y M P K K A T E L K Q L Q C L E E E L K P

TCTGGAGGAAGTGTGAAATTAGCTAAAGCAAAACTTCACTTAAGACCCAGGGACTTAATCAGCAATATCACGTAATAGT
AGACCTCCTCACGACTAAATCGAGTTCGTTTGAAAGTGAATTCTGGTCCCTGAATTAGTCGTTAGTTGCATTATCA
> L E E V L N L A Q S K N F H L R P R D L I S N I N V I V

TCTGGAACCTAAAGGGATCTGAAACACATTCACTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTCTGAACAGATG
AGACCTGATTCCCTAGACTTGTGTAAGTACACACTTACGTCTACTCTGTCGTTGGTAACATCTAAAGACTTGTCTAC
> L E L K G S E T T F M C E Y A D E T A T I V E F L N R W

```

**FIGURE 5**

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GATTACCTTGTCAAAGCATCATCTAACACTAACTTGATTTTGT<sub>a</sub>GATCTGTCGACCATTAGTATCCTAAAATTGAA  
 CTAATGGAAAACAGTTCTGAGTAGAGTTGTGATTGAAC<sub>AAAAACA</sub>tCTAGACAGCTGGTAAATCATAGGATTTAACTT  
 > I T F C Q S I I S T L T . FPV early/late  
 promoter

Early transcriptional  
stop sequence (bold)

TTGTAATTATCGATAATAATGAGAGCTGTCCCTCTGCACCTCGTCGGGACAGCAAGCCTCACCCCTGGCTCTTGCTCTGCT  
 AACATTAATAGCTATTATTTACTCTCGACAGGGAGACGTGGAGCAGCCCTGTCGGAGTGGAAACCGAAGAACGAGGACGA  
 > M R A V P L H L V G T A S L T L G F L L L L  
 Rat PAP protein coding sequence

ATCTCTCCGCCCTGGACCCAGGCCAAGCCAAGGGAGTTGAAGTTGTGACATTGGTGTCCGGCATGGAGACCGAGGTCCCACATCGA  
 TAGAGAGCCGGACCTGGGTCGGTCTCAACTTCAAACACTGTAACCACAAGGCCGTACCTCTGGCTCCAGGGTAGCT  
 > S L R L D P G Q A K E L K F V T L V F R H G D R G P I E

GACCTTCTAATGACCCATTAAGGAATCCTCGTGGCCACAAGGATTGGCCAACTCACCAAGTGGGATGGGACAGCACTA  
 CTGGAAAGGATTACTGGGTAATTCTTAGGAGCACCGGTGTTCTAAACCGGTTGAGTGGTTACCCCGTACCCCTGTCGTGAT  
 > T F P N D P I K E S S W P Q G F G Q L T K W G M G Q H Y

CGAACTCGGAAGTTATATAAGGAGAAGATAACGGGAGATTCTGAACAACTCCTATAAACATGACCAAGGTTTATATCCGAAGCAC  
 GCTTGAGCCTCAATATATTCTCTATGCCCTCTAAAGAACTTGTGAGGATATTGTACTGGTCAAATATAGGCTTCGTG  
 > E L G S Y I R R R Y G R F L N N S Y K H D Q V Y I R S T

AGATGTTGACAGGACTCTGATGAGCGCTATGACAAACCTCGCACGCCCTGTTCCCCCTGAGGGGATCAGCATCTGGAATCCCG  
 TCTACAACTGTCCTGAGACTACTCGCGATACTGTTGGAGCGTCGGACAAAGGGGACTCCCTAGTCGTAGACCTTAGGGC  
 > D V D R T L M S A M T N L A A L F P P E G I S I W N P R

ACTGCTCTGGCAGCCCATCCAGTGACACCGTGTCTCTCTGAGGATCGGTTGCTATACCTGCTTCAGGGACTGTCCTCG  
 TGACGAGACCGTGGTAGGGTCACGTGTCGGCACAGAGAGAGACTCCTAGCCAACGATATGGACGGAAAGTCCCTGACAGGAGC  
 > L L W Q P I P V H T V S L S E D R L L Y L P F R D C P R

CTTCAAGAACTCAAGAGTGAGACTTAAAATCTGAGGAGTTCTGAAGAGGCTTCAACCATATAAGCTCATAGACACCTT  
 GAAAGTTCTTGAGTTCTCACTCTGAATTTAGACTCCTCAAGGACTTCTCGAAGTGGTATATTTCGAAGTATCTGTGAA  
 > F Q E L K S E T L K S E E F L K R L Q P Y K S F I D T L

GCCATCGCTGTCGGGATTGAGGACCAAGGATTTTGAATCTGGAGTAGGCTTACGACCCCTTATATTGCGAGAGTGTCA  
 CGTAGCGACAGCCCTAACGCTCTGGCTTAGAAAAACTTACGCTCATCGAAATGCTGGAAATATAACGCTCTCACAGT  
 > P S L S G F E D Q D L F E I W S R L Y D P L Y C E S V H

CAATTCACCTTCCGCACCTGGGCCACAGAGGACGCCATGACTAAGTGAAGGAGTTGTCAGAATTATCTCTGTTATCTCTT  
 GTAAAGTGGAGGCCTGGACCCGGTCTCCTCGGGTACTGATTCAACTCCTCAACAGTCTTAATAGAGACAATAGAGAAAT  
 > N F T F R T W A T E D A M T K L K E L S E L S L L S L Y

TGGAATTCAACAGCAGAAAGAGAAATCTAGACTCCAGGGGGCGCTGGTCAATGAAATTCTCAAGAACATGAAGCTGCAAC  
 ACCTTAAGTGGTCTCGTCTTCTCTTACGATCTGAGGTCCCCCGCAGGACCAAGTTACTTAAAGAGTTCTGTACTTCGAACGTTG  
 > G I H K Q K E K S R L Q G G V L V N E I L K N M K L A T

TCAACCACAGAAGGCCAGGAAGTTGATCATGTATTCTGCATATGACACTACTGTGAGTGGCCTGCAGATGGCGCTAGAGCTT  
 AGTTGGTGTCTCCGGTCTTCAACTAGTACATAAGACGTATACTGTGATGACACTCACCAGCGTCTACCGCGATCTCGAAAT  
 > Q P Q K A R K L I M Y S A Y D T T V S G L Q M A L E L Y

TAATGGACTTCTACCTCCCTACGCTTCTGCCACATAATGAAATTGTCAGGATAATGGGGGACCTTGGAGATGTACTA  
 ATTACCTGAAGATGGAGGGATGCGAAGGACGGTGTATTACCTTAACATGGTCTATTACCCCTGGAGACACCTCTACATGAT  
 > N G L L P P Y A S C H I M E L Y Q D N G G T F V E M Y Y

CCGAAATGAGACCCAGAACGAGCCCTACCCACTCACGCTGCCGGCTGTACCCACAGCTGCCCTCTGGAGAAGTTGCAGAGCT  
 GGCTTACTCTGGTCTGGATGGGTAGTGCAGGGCCCGACATGGGTGTCGACGGAGACCTCTCAAACGCTCGA  
 > R N E T Q N E P Y P L T L P G C T H S C P L E K F A E L

FIGURE 5 cont.

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ACTGGACCCGTGATCCCCAGGACTGGGCCACAGAGTGTATGGGCACAAGCAACCACCAAGCGTCGCTGTAATTTCTGTCG  
 TGACCTGGGGCACTAGGGGTCTGACCCGGTGTCTCACATACCGTGGTGGTTCGAGCAGCATTAAAAGACAGC  
 > L D P V I P Q D W A T E C M G T S N H Q A S L .

ACCCATGGTTGTTAAAAAGGAATTGAAAGAAAAATTTTATCGTAATAAATTAATATGCATGAAGGACATCAGGAGTCTT  
 TGGTACCAACAAATTCTTCTTAACTTCTTATAAAATAGCATTATTAAATTACGTACTCCTGTAGTCCTCAGAAA  
 FPV134R ORF in bold

TAAAGAACCTGAAATGACAAACCTTATATGTTCTCAATGAACTAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTC  
 ATTCTTGAACCTTACTGTTTGGAAATAACAAGAAGTTACCTGATCATCCACTCTCTGTATATTGTTCTCAATCTTTAAG

TAATACTAAGTTCAAGGACAGGGCCAGCTTAAGCTGTTAGGAGAACTTTATTCTTAAATACATTAATCAAGAATAAAAC  
 ATTATGATTCAAAGTTCTGTCCCGGTGCAATTGACAATACTCTTGTAAATAAGAATTATGTAATTAGTTCTTATTTTG

GTTATGTTCAGATACTGTTAGGTCAGCACCAGGAAGCCATATAAATTCTTATCATTATATGGATGA  
 CAATACAAGTCTATGTCAATAGCACATATCCCAGTCGTGGCTTCGGTATATTAAAAAATAGTAATACACTACT

Early transcriptional  
stop sequence for rat PAP

TCTAAAAATAGATTAAATGGATATTAAATAGATGGTAGAGATCATGATCGATCTCTAGAAAGTCTTAAAATGTGTCTATAAT  
 AGAATTCTAAATTACCTATAATTCTACCATCTCTAGTACTAGAGATCTTCAGAATTTCACACAGATATTA

ACATAGCTTGTAGATGAACAATACTGTTAACGCTACGTAAATGATTAGGAAAACCATAAAATTGTACTGATATCAGATA  
 TGTATCCAACATCTACTTGTATGAAACAATTGATGCATTACTAACTCTTGTATTTAACATGACTATAGTCTATA

TAGATCGCTAACAGGAAAAGAACCTACTAGCGAGGACCTATTACACGATTACCGGTGCGAGAATCAAATGGTAAGCATTCTAA  
 ATCTAGCGATTCTCTTCTGGATGATCGCTCTGGATAATGTGCTAATGCGCAACGTCTAGTTACCTCGTAAGAATT

ACCAATAGCATCGAGCCTGAAATGGAGATGTCCGTTCCGGATCAGTGGATAAGAGACTTTACATTCTGTGGAGATGAGTT  
 TGGTTATCGTAGCTCGGACTTACCTCTACAGGCAAAGGCCTAGTCACCTATTCTGTAAAGAACACCTCTACTCAA

T  
A

**FIGURE 5 cont.**

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**Insertion site of VIR502 containing human IL2 and human PAP sequences**

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

**ATGGATAGAAATATCAATTAGCTGTATTAGAACCTAGGTTAACACAGAGTTCTATTATCCTCAAAGGTA**  
**TACCTATCTTATAGTAAATCAGGACATAAATCTGGATCAAATTGTGCTAAAGATAATAGAGGAGTTCCAT**  
 FPV132R ORF in bold →

TTTTATATATTAGTTGAAGTAATAGTAGCTTGATTATATTGAATTTCAGGAAGAAATATTATACAT  
**AAAAATATATAATCAAAAACATTCAATTATCATCGAAACTAATATAACTTAAAAAGAAATTCTCTTATAATATATGTA**

TTTTCCGTTAGCTAAGCTTCTAAAAATTCAATAAAATAGCTGCTGGATAGAACTATGTTAAATGTGAAGAAGATGGA  
**AAAAAGCCAATCGATTGGAAGATTAAAGTTAAGTATTATCAGACGACCTATCTGATACAATTACACTTCTTCTACCT**

TCTTGATGATTCGAGACCTTCCGGTATCTATCGGCCCTGAGTTAGTGGTACCCGTAAGGATTCGATTGTAG  
**AGAAACTACTAAAGCTCGGAAGGCCATAGATAAGCCGAACCTCAAATCTACCAAGTGGCATTCTAAAGGCTAACATC**

TTTGTTTATCGTCAATAAAATGGCCATCTCATCAACATCTCCTTACTCTATTAAACAGACATAACGGATTTTAAACAGACATAACGGATTTTAAACAGAAAATAGCAGTTATTACCGCGTAGGAGTAGTTGAGAGATAAAAATTGTCGCTATTGCCTAAAATA

TCTTATCTATCGAAAAAAAGTGTGATGAAGCTTGTGAAGACATAAAACTATTAAAGAAATATGGACTTTATTCTAAG  
 AGAATAGATAGGTTTTTCACTACTACTTCGAGAACTTCTGTATTATGATAATTCTTATATACCTGAATAAGATT

CGTTCTTATACGTTCTAAAGAGAAACTAGAAAATAGGATGTTCTACGAGCCTATGAGTGAATCGTTAAAGGCTTTA  
 GCAAGAATATGCAAGATTCTCTTGTATCTTATATCCTACAAGAATGCTCGGAACTCACTTAGCAAATTCCGAGAAT

TTAAAGTAAAGGATGATGGTACTTAGTAAAGCATTACCAAGCCATTGTTAAATCCTCATCCGAAAAGATAGTTTA  
 AATTTCATTCTACTACCAGTAAATCGTAAATGGTCGTAACAATTAGGAGTAAGGCTTCTATCAAAT

GATAGAGGTTATACTCGGATTTGTATAAGCGTAATAAGACTATCTAGTAAAGCAGTTATATACTTCCGCAAATAC  
 CTATCTCAAATATGAAGCCTAAAAGATATTGCAATTCTGATAGATCATTCTGTAATATATGAAGGGCGTTATG

AAAATACATAAATCCAAACGAGAATATGTATATAACAAACCTAATACTGAAGCGCAACTAGATCT**TCCAAACCC**  
 TTTTATGTATTAGGTTGCTTACATATATTGTTGAGTATAGTGTGACTTCGCGTGTAGCTAGAAGGTTGG

**ACCCGTTTTATAGTAAGTTTCACCCATAAATAAAATACAATAATTAAATTCTCGTAAAGTAGAAAATATATTC**  
**TGGCGAAAATATCATTCAAAAGGGTATTATTTATGTTATAATTAAAGAGCATTTCATTTTATATAAG**  
 vaccinia p7.5 promoter in bold & italic →

**TAATTTATTGCACGGCTAGAACTAGTGatccATGTACAGGATGCAACTCCTGCTTGCATTGCACTAATTCTTGCACT**  
**ATAAATAACGTGCCAGATCTGATCAC<sub>c</sub>taggtACATGTCCTACGTTGAGGACAGAACGTAACGTGATTAAGAACGTGA**  
 > M Y R M Q L L S C I A L I L A L  
 Human IL2 protein coding sequence →

TGTCACAAACAGTGCACCTACTTCAAGTTGACAAAGAAAACAAAGAAAACACAGCTACAACTGGAGCATTACTGCTGG  
 ACAGTGTTGTCACGTGGATGAAGTCAAGCTGTTCTTTGTTGTCGATGTTGACCTCGTAAATGACGACC  
 > V T N S A P T S S S T K K T K K T Q L Q L E H L L L

ATTTACAGATGATTGAAATTAAATTACAAGAACCTTACCCAAACTCACCAGGATGCTCACATTAAAGTTTACATG  
 TAAATGTCTACTAAACCTACCTTAAATTAAATGTTCTAGGTTGAGTGGTCTACGAGTGTAAATTCAAATGTAC  
 > D L Q M I L N G I N N Y K N P K L T R M L T F K F Y M

CCCAAGAAGGCCACAGAACTGAAACAGCTTCAGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTAGC  
 GGTTCTCCGGTGTCTGACTTTGTCGAAGTCACAGATCTTCTCTGAGTTGGAGACCTCCTCACGACTTAAATCG  
 > P K K A T E L K Q L Q C L E E E L K P L E E V L N L A

TCAAAGCAAAAACCTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGTCTGGAACATAAGGGATCTG  
 AGTTTCGTTTTGAAAGTGAATTCTGGTCCCTGAATTAGTCGTTAGTTGCAATTCAAGACCTGATTCCCTAGAC  
 > Q S K N F H L R P R D L I S N I N V I V L E L K G S

**FIGURE 6**

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AAACAACATTCACTGTGTGAATATGCAGATGAGACAGCAACCATTGAGAATTTCTGAACAGATGGATTACCTTTGTCAA  
 TTTGTTGTAAGTACACACTTACGTCTACTCTGTCGGTAACATCTAAAGACTTGCTACCTAATGGAAAACAGTT  
 > E T T F M C E Y A D E T A T I V E F L N R W I T F C Q

AGCATCATCTAACACTAACTTGATTTTG**T**aGATCTGtcgaccat~~ttagt~~**c**taaaattgaattgtattatcg  
 TCGTAGTAGAGTTGTGATTGA**A**AAA**A**C**a**ctTAGACagctggtaatcataggat**ttaacttaacat**taatagc  
 > S I I S T L T . FPV early late promoter →  
 Early transcriptional in bold & italic  
 stop sequence in bold

ataataa**AT**GAGAGCTGCACCCCTCCTCCTGGCCAGGGCAGCAAGCCTAGCCTGGCTTCTGTTCTGCTTTTCT  
 tattatt**T**ACTCTCGACGTGGGGAGGAGGACCGTCCCGTGGATCGGAACCGAAGAACAAAGACGAAAAAGA  
 > M R A A P L L L A R A A S L S L G F L F L L F F  
 Human PAP protein coding sequence →

GGCTAGACCGAAGTGTACTAGCCAAGGGAGTTGAAGTTGTGACTTGGTGTTCGGCATGGAGACCGAAGTCCCATTGAC  
 CCGATCTGGCTTCACATGATCGTCTCAACTCAAACACTGAAACCACAAAGCGTACCTCTGGCTTCAGGGTAAC**T**G  
 > W L D R S V L A K E L K F V T L V F R H G D R S P I D

ACCTTTCCC**A**CTGACCC**C**ATAAAAGGAATCCTCATGGCCACAAGGATTGGCAACTCACCCAGCTGGCATGGAGCAGCA  
 TGGAAAGGGT**G**ACTGGGTATTCTCTAGGAGTACCGGTGTCTAAACGGTTGAGTGGT**C**ACCTCGT**C**GT  
 > T F P T D P I K E S S W P Q G F G Q L T Q L G M E Q H

TTATGAAC**T**GGAGAGT**T**ATAAGAAAGAGATATAGAAA**A**CT**T**CTGAAT**G**AG**T**C**C**TATAAA**A**C**T**GAACAGGTT**T**AT**T**AT**T**  
 AATACT**T**GAAC**C**CT**T**CT**C**AT**A**T**A**T**T**CT**C**T**A**T**A**T**T**AA**G**AA**C**TT**A**CT**C**AG**G**AT**A**TT**T**GT**A**CT**T**GT**C**AA**A**AT**A**AA**A**  
 > Y E L G E Y I R K R Y R K F L N E S Y K H E Q V Y I

GAAGCACAGACGTTGAC**CG**GA**CT**TTGAT**G**AG**T**G**C**TAT**G**AC**AA**AC**C**T**GG**CAG**CC**T**GT**TT**CC**CCAGAAGGT**G**T**C**AG**C**AT**C**  
 CCT**CG**T**G**T**C**GA**CT**GG**C**T**G**AA**AC**TA**C**ACT**C**AC**G**AT**A**CT**G**TT**GG**AC**GG**T**CG**GG**AC**AA**AG**GG**GG**T**CT**CC**AC**AG**T**CG**T**  
 > R S T D V D R T L M S A M T N L A A L F P P E G V S I

TGGAA**T**CT**C**T**A**T**C**ACT**C**T**GG**CAG**CC**CAT**CC**GG**T****G**CAC**AC**AG**T**CC**C**T**TT**CT**G**AAG**A**T**C**AG**T**GT**C**T**A**C**T**GC**CT**  
 AC**C**T**T**AG**G**AT**A**GG**G**T**G**AG**A**CC**G**T**CG**GT**AG**GG**C**AC**G**T**GT****C**A**GG****G**A**AA****A**ACT**T**CT**G**AT**C**A**AC****G****A**T**T**GG**A**CG**GG****A**  
 > W N P J I L L W Q P I P V H T V P L S E D Q L L Y L P F

CAGGA**A**CT**CC**CT**C**GT**TT**CA**AG****A**CT**T**GAG**G**AG**A**CT**T**G**A**AT**C**AG**G**GA**AT****T**CC**A**AG**A**GG**G**T**C**AC**CC**T**T****A**  
 GT**C**CT**T**G**A**CG**GG****A****CA**AA**A**GT**T**CT**G**A**CT****T**C**A**CT**T**G**A**AC**T**TTAG**T**CT**C**TT**A**AG**G**T**C**TC**CC**G**A**CG**T**GG**A****AT****A**  
 > R N C P R F Q E L E S E T L K S E E F Q K R L H P Y

AGGAT**TT**TATAG**C**TAC**C**CT**GG**AAA**A**CT**T**CAG**G**ATT**A**C**T**GG**C**AG**G**AC**C**T**TT**GG**A**TT**T**GG**A**GT**A**AG**T**C**T**AC**G****A**  
 TC**C**TA**AA**AT**A**T**C**G**A**T**GG**AC**CC**T**TT**GG**A**AG**T**C**C**T**A**T**G**T**A**CC**GG**T**C**T**GG**AAA**A**CT**T**AA**C**T**T**C**A**G**A**T**G****C**  
 > K D F I A T L G K L S G L H G Q D L F G I W S K V Y D

CCT**T**TAT**A**T**T**GT**G**AG**G**T**T**C**A**CA**A**TT**C**ACT**T**TAC**C**C**C**T**GG**CC**A**CT**G**AG**G**AC**A**CC**A**T**G**ACT**A**AG**T**GT**G**AG**G**A**AT**  
 GG**AA**AT**A**TA**A**CT**T**C**A**AG**T**G**T**AA**A**GT**G**AA**A**GG**G**AC**CC**GG**T****G**ACT**C**T**GT**GG**T****A**CT**G**AT**C**A**CT****T****C****T****A**  
 > P L Y C E S V H N F T L P S W A T E D T M T K L R E L

GT**C**AG**A**ATT**T**GT**C**CT**C**T**GT**CC**C**T**A**T**G**GA**A**TT**C**AC**A**AG**C**AG**A**AA**A**AT**T**AG**G**C**T**CC**A**AG**GG**GT**T****C**CT**GG**T**C**  
 CAG**T**CT**A**AC**AG**GG**G**AG**A**AC**T**TA**A**GT**G**T**T**CG**T**CT**T**CT**T**AG**A**T**C**CG**A**GG**T****T****CC**CC**A**CG**G**AC**A**G**T**  
 > S E L S L L S L Y G I H K Q K E K S R L Q G G V L V

AT**G**AA**A**AT**C**CT**C**AA**A**CT**C**AC**A**GA**AG**AG**C**AA**C**T**C**AG**A**AC**A**AG**C**T**A**CA**A**AA**A**AA**A**CT**T**AT**C**AT**G**T**A**TT**T**GT**C**C**A**T**G****A**  
 T**A**CT**T**TAG**G**AG**T**TAG**T**G**A**CT**T**C**T**CG**T**GT**G**AT**G**TT**T**GA**A**AG**T**A**C**AT**A**AG**C**G**G**T**A**CT**G**T**G**  
 > N E I L N H M K R A T Q I P S Y K K L I M Y S A H D T

ACT**G**T**G**AG**G**C**T**AC**A**G**A**T**G**G**C**T**A**G**A**T**G**T**T**T**A**C**A**CG**G**A**C**T**C**C**T**CC**C**T**A**T**G**C**T**GT**C**C**A**T**T**  
 TG**A**CA**C**T**C**AC**GG**G**A**T**G**T**C**AC**C**CG**G**A**T**C**A**AA**A**T**G**T**G**C**T**GT**G**AG**G**AG**G**A**T**AC**G**A**G**A**C**GG**T****G**A**A**CT**G**C**T****A**  
 > T V S G L Q M A L D V Y N G L L P P Y A S C H L T E L

**FIGURE 6 cont.**

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GTACTTGAGAAGGGGGAGTACTTGTGGAGATGTAATCGGAATGAGACGCAGCAGGCCGTATCCCTCATGCTAC  
 CATGAAACTCTCCCCCTCATGAAACACCTCTACATGATAGCCTACTCTCGCTCGTCGGCATAGGGAGTACGATG  
 > Y F E K G E Y F V E M Y Y R N E T Q H E P Y P L M L

CTGGCTGCAGCCCTAGCTGCCTCTGGAGAGGTTGCTGAGCTGGTGGCCCTGTGATCCCTCAAGACTGGTCCACGGAG  
 GACCGACGTCGGGATCGACAGGAGACCTCTCAAACGACTCGACCAACCGGGACACTAGGGAGTTCTGACCAGGTGCCTC  
 > P G C S P S C P L E R F A E L V G P V I P Q D W S T E

TGATGACCACAAACAGCCATCAAGGTACTGAGGACAGTACAGATTATTTCTGTCGACCCATGGTTGTTAAAAAGGA  
 ACATACTGGTGGTGTGGTAGTCCATGACTCCTGTCTGTAATTAAAAGACAGCTGGTACCAACAATTTCCT  
 > C M T T N S H Q G T E D S T D \*

ATTGAAAGAAAATATTTATATCGAATAAAATTAAATATGCATGAAGGACATCAGGAGTCTTTAAAGAACATTGAAATGA  
 TAACTTCTTTATAAAATATAGCATTATTAATTACGTACTCCTGTAGTCCTCAGAAAATTCTGAACATTACT  
 FPV134 ORF in bold →

CAAAAACCTTATATGTTCTCAATGAACACTAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTCTAATACTAAGTT  
 GTTTGGAATATAACAAGAAGTTACTTGATCATCCACTTCTGATATTGTTCTCAATCTTTAAGATTATGATTCAA  
 CAAGGACAGGGCCAGCTTAAAGCTTATTAGGAAACTTTATTTCTAAATACATTAATCAAGAATAAAACGTTATGTT  
 GTTCTGTCCGGTCAATTGACAATAATCCTCTGAAATAAAGAATTATGTAATTAGTTCTTATTTGCAATACAAG  
 AGATAACAGTTATCGTGTATATAGGGTCAGCACCCAGGAAGCCATATAAAATTTTTATATGGATGATCTTA  
 TCTATGTCAATAGCACATATATCCCAGTCGTGGCTTCGGTATATTAA**AAAAAATATAGTAA**TACCTACTAGAAAT

Early transcriptional  
 stop sequence in bold  
 for human PAP sequence

AAATAGATTAAAATGGATATTAATAGATGGTAGAGATCATGATCGATCTAGAAAGCTTAAAATGTGTCTATAATA  
 TTTATCTAAATTTCACCTATAATTATCTACCATCTCTAGTACTAGCTAGAGATCTTCAGAATTTCACACAGATATTAT

CATAGGTTTAGATGAACAATACTTGTAAAGCTACGTAATATGATTAGGAAAACCATAAAATTGTACTGATATCAGA  
 GTATCCAAACATCTACTTGTATGAACAAATTGATGCCATTATACTAATCCTTTGGTATTAAACATGACTATAGTCT

TATTAGATCGCTAACAGGGAAAAGAACCTACTAGCGAGGGACCTATTACACGATTACCGTTGCAGAATCAAATGGTAAGCA  
 ATAATCTAGCGATTCTCCTTTCTGGATGATCGCTCTGGATAATGTGCTAATGCGAACGTCTAGTTACCTATTCTG

TTCTTAAACCAATAGCATCGAGCCTGAAATGGAGATGTCGTTCCGGATCAGTGGATAAGAGACTTTACATTCTG  
 AAGAATTGGTTATCGTAGCTCGACTTACAGGCAAAGGCCTAGTCACCTATTCTGAAAATGTAAGGAACA

GGAGATGAGTT  
 CCTCTACTCAA

FIGURE 6 cont.

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## Amino acid sequence alignment of rat PAP from VIR501 with human PAP from VIR502

Boxed: Identical amino acid

10	20	30	
1 M R A V P L H I V G T A S I L T L G F L I I L I S L R L D P G D		A K E L K F V T	LratPAP aa seq
1 M R A A P L L I A R A A S I S L G F I E L I F F V L D R S V		A K E L K F V T	LhuPAP aa seq
<hr/>			
40	50	60	70
40 V F R H G D R G P I E T F P N D P I K E S S W P Q G F G Q L T K N G M G Q H Y			EratPAP aa seq
41 V F R H G D R S P J D T F E T D P I K E S S W P O G F G O L T Q I G M E O H Y			EhuPAP aa seq
<hr/>			
80	90	100	110
80 L G S Y I R R R Y G R F L N N S Y K H D Q V Y I R S T D V D R T L M S A M T N			LratPAP aa seq
81 L G E Y I R R K R Y R K F L N E S Y K H D Q V Y I R S T D V D R T L M S A M T N			LhuPAP aa seq
<hr/>			
120	130	140	150
120 A A L F P P E G I S I W N P R L L W Q P I P V H T V S L S E D P R L L Y L P F R			DratPAP aa seq
121 A A L F P P E G V S I W N E I L L W Q P I P V H T V P L S E D D O L L Y L P F R			NhuPAP aa seq
<hr/>			
160	170	180	190
160 C P R F Q E L K S E T L K S E E F I L K R I L O P Y K S F I D T L P S L S G F E D			QratPAP aa seq
161 C P R F Q E L E S E T L K S E E R K R I L O P Y K S F I D T L G K L S G L H G			QhuPAP aa seq
<hr/>			
200	210	220	230
200 D L F E I W S R L Y D P L Y C E S V H N F T F R T W A T E D A M T K L K E L S			EratPAP aa seq
201 D L F E G I W S K V X D P L Y C E S V H N F T L P S W A T E D T M T K L R E L S			EhuPAP aa seq
<hr/>			
240	250	260	270
240 L S L L S L Y G I H K Q K E K S R L Q G G V L V N E I L K N M K L A T O P O K			AratPAP aa seq
241 L S L L S L Y G I H K Q K E K S R L Q G G V L V N E I L N H M K R A T O I P S			YhuPAP aa seq
<hr/>			
280	290	300	310
280 R K L I M Y S A Y D T T V S G L Q M A L E I Y N G L L P P Y A S C H I M E L Y			QratPAP aa seq
281 K K L I M Y S A H D T T V S G L O M A I D V Y N G L L P P Y A S C H I L E L Y			FhuPAP aa seq
<hr/>			
320	330	340	350
320 D N G G T F V E M Y Y R N E T O N E P Y P I L T L P G C T H S C P L E K F A E L			LratPAP aa seq
321 E K G E Y F V E M Y Y R N E T G H E P Y P I N L P G C S P S C P L E R F A E L			VhuPAP aa seq
<hr/>			
360	370	380	
360 D P V I P Q D W A T E C M G T S N H O A S I			ratPAP aa seq
361 G P V I P Q D W S T E C N T I N S H O G T E D S T D			huPAP aa seq

Decoration 'Decoration #1': Box residues that match ratPAP aa seq exactly.

FIGURE 7

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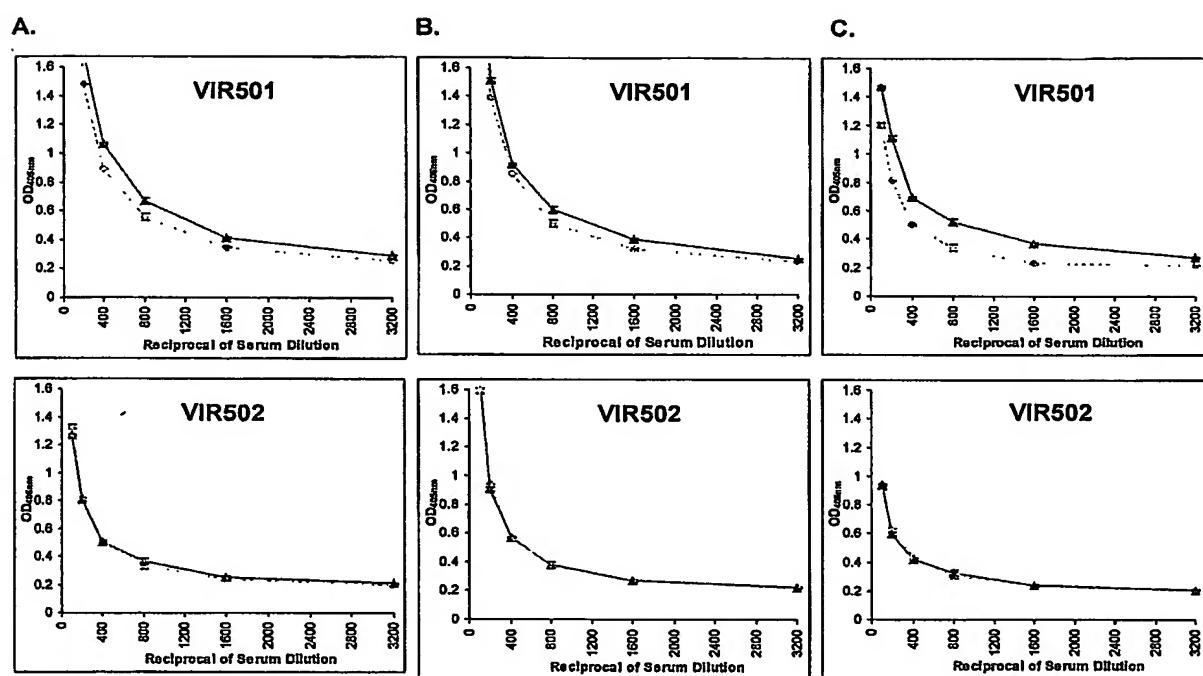
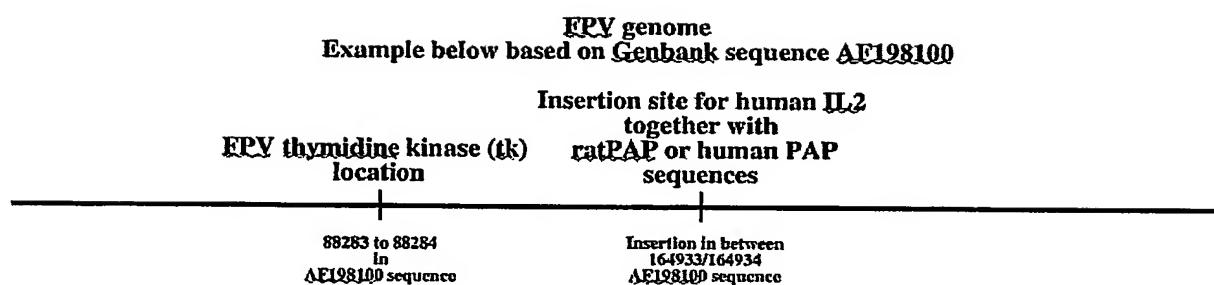
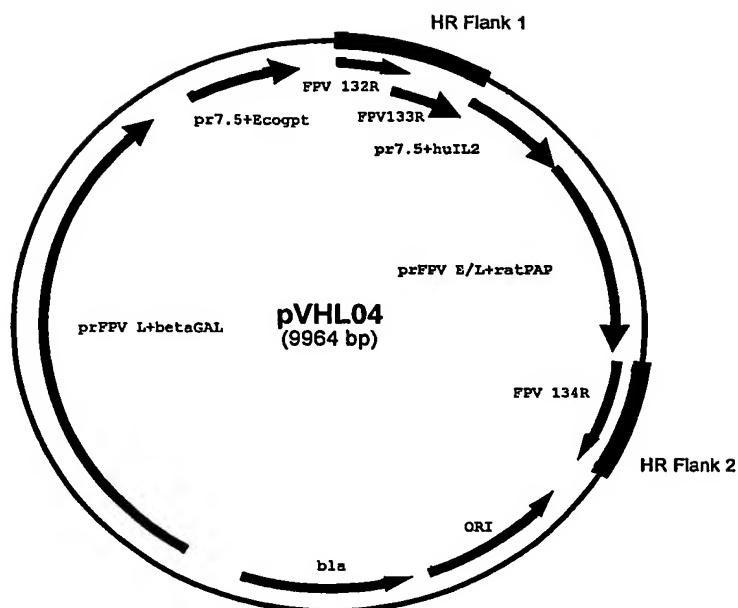


FIGURE 8

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**FIGURE 9**

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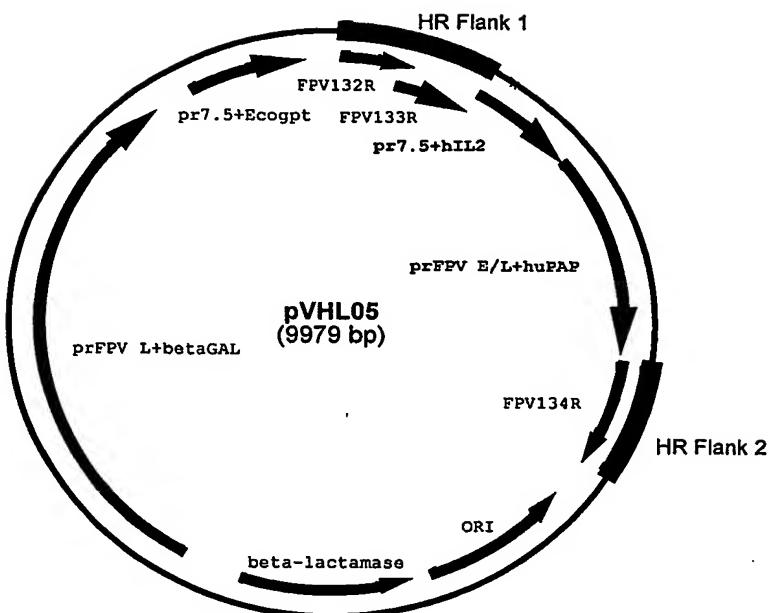


**pVHL04 was constructed by cloning the following into a bacterial plasmid vector:**

1. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
2. pr7.5+Ecogpt: *E coli* xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
3. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs overlap each other. This sequence forms the homologous recombination flank 1.
4. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
5. prFPV E/L+rat PAP: rat prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
6. Fowlpox Virus nucleotide sequence spanning ORFs 134 - this sequence forms the homologous recombination flank 2.

**FIGURE 10**

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**pVHL05 was constructed by cloning the following into a bacterial plasmid vector:**

7. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
8. pr7.5+Ecogpt: E coli xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
9. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs overlap each other. This sequence forms the homologous recombination flank 1.
10. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
11. prFPV E/L+huPAP: human prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
12. Fowlpox Virus nucleotide sequence spanning ORFs 134 - this sequence forms the homologous recombination flank 2.

**FIGURE 11**